An unusual case of pulmonary hypertension with multiple osteosclerotic lesions


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Case report

A 47-year-old married woman with underlying sensorimotor polyneuropathy presented to our emergency department with a 2-week history of fatigue, legs edema and exertional dyspnea. On physical examination, elevated jugular vein pressure, a grade III pansystolic murmur at the left lower sternal border and peripheral edema were noted. Chest radiography revealed cardiomegaly, enlargement of the central pulmonary vessels and bilateral pleural effusions (Figure 1). Electrocardiograms showed right axis deviation. An echocardiogram demonstrated pericardial effusion, severe tricuspid regurgitation, pulmonary hypertension (pulmonary artery pressure was 78 mmHg) and normal left ventricular systolic function (the estimated ejection fraction was 77%). Contrast-enhance chest CT showed no evidence of intraluminal thrombi in the pulmonary arteries but central pulmonary artery dilatation (Figure 2). Chest CT image in a bone window setting showed osteosclerotic lesions in the vertebral body of the thoracic spine (arrow head) and sternum (white arrow), as well as proliferative new bone formation over the right transverse process (black arrow) (Figure 3). She was admitted and initially treated as having pulmonary hypertension with right heart failure.

After admission, poor response to medication persisted. A series of investigations were arranged with the findings as follows. 18F-fluorodeoxyglucose whole-body PET/CT scan and Ga-67 tumor survey revealed no abnormal signal uptake. Diagnostic thoracentesis showed transudate effusion. Serum IgG was 3200 mg/dl (normal range 800–1700 mg/dl). Serum and cerebrospinal fluid protein electrophoresis and immunoelectrophoresis showed a monoclonal spike of IgG-lambda. Bence Jones protein tests were negative. Endocrinology was unremarkable. The combination of polyneuropathy with monoclonal gammopathy, osteosclerotic bone lesions and pleural effusions led us to consider a diagnosis of POEMS (polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes) syndrome. After 3 weeks of prednisone 1 mg kg/day treatment, clinical symptoms resolved dramatically. Pulmonary artery pressure decreased to 22 mmHg, as assessed by echocardiogram. The dose of prednisone was gradually decreased to 20 mg/day. Two years later, a marked improvement in the neuropathy was noted and there was no recurrence of pulmonary hypertension.

POEMS syndrome is a paraneoplastic syndrome due to an underlying plasma cell neoplasm. The major criteria for the syndrome are polyneuropathy, clonal plasma cell disorder, sclerotic bone lesions, elevated vascular endothelial growth factor (VEGF) and the presence of Castleman disease. Minor features include organomegaly,
endocrinopathy, characteristic skin changes, papilledema, extravascular volume overload and thrombocytosis. The diagnosis of POEMS syndrome is made with three of the major criteria, two of which must include polyneuropathy and clonal plasma cell disorder, and at least one of the minor criteria (Table 1).

Pulmonary manifestations of POEMS syndrome are protean, including pleural effusions, pulmonary hypertension, restrictive lung disease, impaired diffusion capacity of carbon monoxide and impaired neuromuscular respiratory function, but improve with effective therapy. In a series of 99 patients with POEMS, 36% manifested pulmonary hypertension. Overproduction of cytokines is probably involved in the pathophysiology of pulmonary hypertension.

There are two skeletal manifestations of POEMS syndrome: focal bone lesions and proliferative new bone formation. These lesions are often osteosclerotic, as seen in Figure 3. The diagnosis of POEMS syndrome is confirmed when both of the mandatory major criteria, one of the three other major criteria, and one of the six minor criteria are present. Adapted from Dispenzieri (2007)
bone formation.\textsuperscript{5–7} Focal bone lesions occur in \textasciitilde95\% of the patients. The pelvis, spine, ribs and proximal extremities are most often involved. Bone pain and pathological fractures are rare. In our case, multiple sclerotic bone lesions in the spine and sternum were easily regarded as osteoblastic metastases. The other differential diagnoses include lymphoma, osteosclerotic variants of multiple myeloma, mastocytosis and myelofibrosis.\textsuperscript{8}

Proliferative new bone formation is seen at both axial and extra-axial sites. These proliferative changes are uncommon, but are specific for POEMS syndrome.\textsuperscript{7} In our case, osseous proliferation, especially at the posterior elements of the lumbar spine, has been considered virtually pathognomonic for POEMS syndrome.\textsuperscript{6}

The main therapeutic options for patients with POEMS syndrome include radiation therapy, chemotherapy, corticosteroids, hematopoietic cell transplantation and anti-cytokine/anti-VEGF agents.\textsuperscript{1,9} The osteosclerotic lesions in POEMS are a criterion for both diagnosis and staging of the disease, as well as an index for determining the choice of therapeutic approach. The number and size of the bone lesions are the main quantitative objective variable indicating the volume of the plasma cell mass. Single or multiple osteosclerotic lesions in a limited area should be treated with radiation. If a patient has widespread osteosclerotic lesions or diffuse bone marrow plasmacytosis, systemic therapy is warranted. In addition, steroid treatment should be used as first-line therapy in POEMS syndrome-related pulmonary hypertension.\textsuperscript{10} In our case, the symptoms improved dramatically together with decrease in pulmonary artery pressure after treating with steroid.

In conclusion, POEMS syndrome is rare and diagnosis of patients with POEMS is frequently delayed because of protean clinical manifestations. One of the greatest practical challenges for treating physicians is making the diagnosis in a timely fashion to prevent severe irreversible neurological disability. Keeping a high index of suspicion in those with unexplained osteosclerotic bone lesions, pulmonary hypertension and pleural effusions, which can be easily detected by radiography and CT, is therefore essential. This report indicates that early recognition of the link between unexplained osteosclerotic lesions in the skeleton and pulmonary hypertension and polyneuropathy can lead to an accurate and early diagnosis of POEMS syndrome in primary care settings.

\textit{Conflict of interest:} None declared.

\textbf{References}